EUROPEAN PATENT APPLICATION

(i) Application number: 93115730.9

3

- (6) Int. CLS, A61L 29/00, A61L 33/00 (a) Date of filing: 29.09.93
- A request for addition of the description has been filed pursuant to Rule 88 EPC. A decision on the request will be taken during the proceedings before the Examining Division (Guidelines for Examination in the EPO, A-V,
- Priority: 30.09.92 US 954906
- Date of publication of application: 20.04.94 Bulletin 94/16 **②**
- Designated Contracting States: BE DE ES FR GB NL 3

- 730 Central Avenue Murray Hill New Jersey 07974(US) Applicant: C.R. BARD, INC. ⑤
- Inventor: Elton, Richard K. Still River, Mass.(US) Glens Falls, N.Y.(US) 8 Wing Street
- Widenmayerstrasse 23 D-80538 München (DE) **②**
- Process for preparing functionally coated expanded products from expandable tubing and the expanded products produced thereby.
- solvent. Conventional fabricating procedures are used for stretching and expanding the coated tubing. tional agent (e.g., poly(ethylene oxide), a hydrophilic polyurethane or polysiloxane) dispersed, or emulsitied in a carrier such as water and/or an organic Optional steps may include a heating step during stretching and expansion. The coated products produced by this process have an uniformly functional (9) A process for preparing expanded thermoplastic medical products (e.g., dilatation balloons) having biomedical functional coatings such as lubricous coatings or protective coatings is disclosed. The process involves the steps of coating a suitable expandable thermoplastic tubing with the blomedical functional coaling, at least partially drying the coated lubing, and then stretching and expanding the coated tubing. The coating comprises at least one func-FP 0 592 870 A3

- Inventor: Tedeschi, Eugene 216 Still River Road **®**
- Representative: Laufhütte, Dieter, Dr.-Ing. et al Lorenz-Seldier-Gossel

BEST AVAILABLE COPY

EP 0 592 870 A1

BACKGROUND OF THE INVENTION

tic medical products, particularly to a novel process for praparing an expanded thermoplastic medical hered to the expanded surface, particularly coated product having a functional biomedical coating ad-This invention relates to expanded thermoplasballoons for use on catheters.

at Col. 4, lines 48-54 and exemplified at Col. 5, lines 41-44 of U.S. 5,026,607 (ssued June 25, 1991 to M. Klezulas). The dilatation balloons are bonded to an appropriate catheter shaft using an coatings to balloons utilizes the step of applying the coating to the pre-formed balloon, i.e., to the blow molded balloon. Preferably the coating is applied to the inflated pre-formed balloon. Applying tion of a coating layer having a generally uniform thickness. A typical coating procedure is described first formed from the appropriate tubing by a series of stretching, optionally heating, and expanding op-erations such as blow molding. Then the balloon is adhesive or other appropriate means. Alternatively the tubing may be an integral part of the catheter. Finally, the functional coatings are applied, typically by dipping or spraying. The coated surface is althe coating to the inflated balloon allows the forma-The prior art process for applying functional

and alter the physical properties, e.g., by changing Current functional coatings used on pre-formed balloons are generally limited to water borne dispersions and emulsions because most organic solvents tend to permeate the thin wall of the balloon towed to dry and cured if necessary. the polymer crystallinity.

There are several disadvantages to coating processes which involve applying the functional coating to a pre-formed balloon. These disadvantages include the following:

objects can be inconsistent due to non-uniform drainage of the coaling solution as it flows off (i) the coating thicknesses on irregularly shaped the coated object, and some balloon geometries may promote entrapment of air during coaling. thus producing a product with cosmetic irregularities;

crystalline and thus are very sensitive to changes caused by contact with the solvents present in some coaling solutions; and are also (ii) pre-formed balloons are highly oriented and sensitive to any heating operations that may be required for curing a coating or driving off sol-

20

apply the coating by spraying rather than dip-ping, in which case there are safety concerns with flammability, exposure to the finely divided solvent mist, and unwanted side effects on the pre-formed balloons it may be necessary to (iii) to minimize the effect of solvent exposure on

coating due to evaporative cooling of the linely divided droplets formed during spraying: and (iv) the high value loss of coated pre-formed balloons and coated finished catheters which are caused by coating errors.

SUMMARY OF THE INVENTION

for a medical product with a coating containing a functional biomedical material and a carrier and to It is an object of the invention to coat an expandable thermoplastic tubing material suitable then expand the coated tubing to form an expanded medical product with an adherent coating of the functional biomedical material. 5

It is a further object of the invention to coat an expandable thermoplastic tubing suitable for blow It is also an object of this invention to coat an expandable thermoplastic tubing suitable for foruniformly functional, highly adherent coating on its molding a dilatation balloon with a lubricious coatming a balloon with a coating which contains a functional blomedical material and to expand the coated tubing to form an expanded balloon with a outer surface.

8

ing and to blow mold the coated tubing to form a subrictious dilatation balloon.

ĸ

(a) applying to at least a portion of an inner and/or an outer surface of an expandable thermoplastic tubing at least one adherent functional biomedical coating which comprises at least one The present invention provides a process for preparing a coated expanded thermoplastic medical product. The process comprises the steps of:

and temperature sufficient to remove at least (b) allowing the coated tubing to dry at a time functional agent and a carrier; part of the carrier; and

(c) stretching and/or expanding the dried coated tubing with an inflating fluid at a pressure suffimedical product. The expanded thermoplastic medical products prepared by this process are cient to form the functionally coated expanded uniformly functionally coaled.

\$

The present invention provides a process for preparing a coated balloon. The process comprises

£

(a) applying to at least a portion of an inner and/or an outer surface of an expandable thermoplastic tubing at least one adherent functional biomedical coaling which comprises at least one

and temperature sufficient to remove at least (b) allowing the coated tubing to dry at a time-(c) stretching and/or expanding the dried coated

tubing with an inflating fluid et a pressure suffi-cient to form the functionally coated balloon.

Rank Xerox (UK) Business Services

The present invention also provides a process preparing a lubricious dilatation balloon. The

poly(ethylene oxide) dissolved, dispersed, or selected from the group consisting of a polyurethane, a polyurea, and a polyurethane-urea or polymer precursors selected from the group consisting of polyurethane precursors and polyurea precursors, the polymer or polymer precursors being dissolved, dispersed, or emul-(a) applying to at least a portion of an outer surface of an expandable thermoplastic tubing at emulsified in the carrier, and (iii) a polymer least one adherent functional biomedical coaling which comprises (i) one or more carriers. (ii) a process comprises the steps of:

and temperature sufficient to remove at least (b) allowing the coated tubing to dry at a time part of the carrier; and sified in the carrier(s);

20

third in order to increase the diameter and length of the tubing while simultaneously orienting the tubing. The fubricious dilatation balloons prepared by this process are uniformly function-(c) expanding the coated tubing with an inflating ally coated.

22

As used herein, the term "thermoplastic" is exclusive of natural or synthetic rubbers. It is understood that thermoplastic materials which can be further heat treatment to cure the coating and/or the tubing and form a thermoset tube are also formed into a tube, coated, and then subjected to suitable for use herein.

8

ments. The functional biomedical coatings useful herein must exhibit adhesion suitable for the intended end use of the medical product and they should have the potential for reasonably high radial ings are usually, but not necessarily activated in an ture resistance and/or tear resistance, (ii) functional such as anti-thrombogenic properties, antimicrobial As used herein, the term "functional biomedical coating" is used for coatings applied to medical products intended for use in the body. Such coataqueous environment, and they provide (i) protective properties such as abrasion resistance, puncproperties such as lubricity, thromoboresistance, hemocompatibility, and (iii) therapeutic properties properties and the like, and like functional improveand circumferential stretching.

thermoplastic tubing material being coated in the second The carriers used for the coatings can be either an organic solvent or water, with the choice depending on the coating components and on the some cases one or more organic solvents may be used, whereas in other cases water may be used as the carrier. Suitable solvents are those which do not adversely affect stretching and expanding steps

as ethylene glycol methyl ether; esters such as col monoethyl ether acetate; aromatic and aliphatic solvents such as benzene, toluene, xylene, Nmethylpyrrolidone, and pyridine; nitroparaffins such as 2-nitropropane; chlorinated solvents such as methylene chloride, methylene bromide, trich-loroethylene, ethylene dichloride; and mixtures of the above. The chlorined solvents are particularly from the coated tubing. Suitable solvents include alcohols such as ethanol or ethylene glycol: ketones such as methyl ethyl ketone; ethers such which are used to form the final expanded product ethyl acetate: ether acetates such as ethylene glyuseful for poly(ethylene oxide) containing coatings.

The ability to maintain a continuous coating over the surface of the thus-expanded balloon, even after the radial and circumferential stretching of several hundred percent which is involved in expanding the balloon, is highly advantageous.

Applying the functional biomedical coating to the expandable thermoplastic tubing prior to expansion provides the following advantages:

(i) it is possible to coal the tubing using solvents which would otherwise attack and deform a preformed polymeric material such as a dilatation balloon, thus greatly broadening the range of coatings which can be used;

pre-formed objects such as catheter balloons or assembled catheters with attached balloons; (ii) It is much less expensive to discard rejected coated coated tubing than to discard rejected coated

(iii) it is much easier to control the uniformity of the resulting coating because the material being er than a pre-formed object, such as a balloon, coated, i.e., the tubing is a simple cylinder rathwith a potentially complex geometry:

(v) separately coating the components of a multi-component device allows one to produce a device with different performance properties for unlike pre-formed expanded products such as each component, depending upon the coating on each component, and this cannot be obtained if one is limited to coating the entire (iv) it is possible to readily cure coatings requiring elevated temperatures because the tubing. dilatation balloons or assembled products, can tolerate the significantly higher temperatures required to cure many coating compositions;

more efficient production because it allows size multaneous manufacturing steps to occur in parnents of a multi-component device lends itself to (vi) separately coating the individual compomulti-component device; and allel rather than in series.

DESCRIPTION OF THE PREFERRED EMBODI-MENTS

EP 0 592 870 A1

BEST AVAILABLE COPY

viny chorlds; copolyssiers; silicone polycarbonate copolymers; ephylene-vinyl acetate copolymers; polyeting polyeting tolyamide block copolymers such as pebase; oxlycarbonates; innomers such as Suriyer; polybutylene terephthalate, polyaryletiter ketones; polytmides; polyamides; pol performance parameters required for the balloon, coating adhesion, and biocompatibility in making The expandable thermoplastic tubings to be coated include tubings made from the materials typically used to form expanded products such as propylene, polyethylene terephthalate or block copolymers thereof admixed with low molecular similar compositions employing butadiane or isoprene in place of the ethylene and butylene; polyomatic polyamides; polyetherimides; polyamideimides; and the like. One skilled in the art will consider such factors as processability. dilatetion belicons, esophageal dilatation balloons, fallopian tube dilatation balloons, peripheral angiopiasty dilatation balloons, prostate dilatation balloons weight styrene and optionally polypropylene, and loons, coronary angioplasty balloons, uterine manipulator balloons and the like, included among the suitable thermoplastic materials are polyurethanes. polyethylene, ethylene-butylene-styrene, poly-

5

5

the appropriate selection.
The choice of diseation balloon material will depend on the particular application. For example, depend on the particular application. For example, some applications will require a rigid non-compliant some applications will require a rigid non-compliant. polymer, while other applications will favor the use of a softer polymer.

of the balloon as well as its elasticity. If the segmented polyurethane to be coated is a hard polymer, then preferably a hard polymer should be used in the functional coaling. If the segmented polyurethane to be coated is a soft polymer, then preferably a softer polymer should be used in the functional coating. Of particular interest for dilatation balloons are certain PELLETHANE® polyure-Segmented polyurethanes can be varied by using different Isocyanates and polyols and different ratos of hard to soft segments in the polymer. The hard to soft ratio defines the expansion capabilities Segmented polyurethanes are suitable as thermoplastic tubing materials for dilatation balloons. hane polymers (e.g., PELLETHANE® 2367-75D).

ene terephthalates (PET), particularly high molecular tar weight homopolymers of 'PET and PET copolyesters. Balloons made from PET tend to be highly rigid when inflated and are capable of sustaining high inflation pressures even when the bal-ing-materials for dilatation balloons are polyethylioon wall thickness is thin, e.g., less than 0.002".

on factors such as the function desired (i.e., lubricity, hemocompatibility, antimicrobial properties, etc.), the ability of a particular coating to bond to the thermoplastic tubing material, the ability of the coating to endure the stretching and/or expanding process, durability (e.g. abrasion resistance) required of the coating in its intended application. and the like. One skilled in the art of coating will weigh these factors in making an appropriate biomedical coatings which can be adapted for use in this process. The choice of coating will depend Similarly, there is a wide range of functional

bogenic. See Chapter 4 "Poly(ethylene oxide) and Related Hydrogels" by Neil B. Graham (pp. 95desirable because poly(ethylene oxide) has the desired functional characteristic of "passivating" a Vol. Il Polymers, ed. by N. A. Peppas, CRC Press, Inc., Boca Raton, Florida, 1986. Coatings containing poly(ethylene oxide) are surface toward platelets and it is quite non-throm-113) in "Hydrogels in Medicine and Pharmacy",

when complexed with a complexing polymer, a high degree of durability. These properties are particularly useful and sought after in dilatation Such coatings provide a combination of useful properties, namely, lubricity, biocompatibility and. balloons.

oxide) and polyurea precursors. Preferred coatings contain poly(ethylene oxide) blended with polyure-(ethylene oxide) and pre-formed polyurethanes. polyureas, or polyurethaneureas are particularly thane precursors which are polymerized and cros-Functional biomedical coatings containing polyuseful, as are coatings containing poly(ethylene slinked in situ on the coated surface.

8

are coalings of the type described in <u>U.S.</u> 5,077,352 (issued December 31, 1991 to R. K. <u>Eiton), the disclosure of which is incorporated here-</u> in by reference. These coatings are applied as a solution of an isocyanate, a polyol, and a high Particularly preferred for applications requiring molecular weight poly(ethylene oxide).

After application of the coating, at least a porpermanent lubricity, coating durability, abrasion resistance and a high poly(ethylene oxide) content

aby, the weight ratio of iscoyanate and polyol 10 poly(ethylene. oxide) varies from 0.25-10 60 and most preferably from 0.75 60 2.0. The stoichiometric ratio of total NCO groups in the isocyanate to total OH groups in the polyol may vary from 0.8 to 3.5, preferably from 0.85 to 1.5. Advantageously, when used as the coating in the cured by allowing the polyol and isocyanate to thane matrix associated or complexed with the tion of the solvent is removed and the coating is react to form a crosslinked substantially polyurepoly(ethylene, oxide), by, hydrogen bonding. Prefer-

present process, the Elton coating not only has the ability to adhesively bond by crosslinking but also the ability to soften, etongale, and conform to the thermoplastic fubring when moderate heat is and expanding of the coated tubing do from a balloon.

The particularly preferred coating of the Elton patent is prepared by weighing appropriate quantities of isocyanie, poiyol, and poly(eithylene ovite), acting them to an appropriate solvent, and adding additional solvent as needed to adjust the adding additional solvent as needed to adjust the solvest is the solvent and adding additional solvent as needed to adjust the solvest. ride, mathylene bromide, dichloroethane, dibromoethane, chlorotorm, and trichloroethylene, and blends of the above. Solids contents in a range solvents for this coating may include acetonitrile, ably halogenated solvents such as methylene chlodioxolane, n-methyl pyrrolidone, pyridine, prefer-

of from 0.4 to 40% are preferred.

Another functional poly(ethylene oxide) coating useful herein is the hydrophilic coating described in U.S. 4,459,317 (ssued July 10, 1984 to H.R. Lambert), the disclosure of which is incorporated herein by reference. A first coating of unreacted pound having at least two unreacted isocyanate pound having at least two unreacted isocyanate groups per molecule and then evaporating of polyvent by air drying. A second coating of poly-(ethylene oxide) dissolved in a solvent is then applied, the solvent is evaporated off, and finally the coating is cured, preferably for 5-30 minutes at 50-100 C in the presence of a water-containing gas such as ambient air. Known isocyanate curing catalysts may be added to one or both coating when the isocyanate groups react with water during the curing to yield an amine which rapidly reacts with other isocyanate groups to form urea crosisocyanate groups on the polymer surface is formed by applying a solution containing a com-(ethylene oxide) - polyurea interpolymer formed solutions. The coating normally consists of a poly-

8

isocyanate compound are ethyl acetate, acetone, chloroform, methyl ethyl ketone, ethylene dichloably 1 to 6% (weight/volume), of the isocyanate Suitable isocyanates include polymethylene polyphenyl isocyanate, 4,4'-diphenylmethane diisocyanate, and 2,4-toluene diisocyanate as well as prepolymers or other addition products of isocyanates and polyols. Suitable solvents for the ride, and preferably methylene chloride. The isocyanate solution may contain 0.5 to 10%, prefer-

ş

The poly(ethylene oxide) used should have a preferably 105. A suitable poly(eithylene oxide) is poly(ethylene oxide) are the same as those under the trade name Polyox® by Union Car-Corp. The preferred and suitable solvents for mean molecular weight of between 10° and 107.

\$3

discussed above. The proportion of poly(ethylene oxide) is preferably between 0.5 and 10%, most preferably between 2 and 8% (weight/volume).

(ethylene oxide) coalings are found in <u>U.S.</u> 4.990.357 (issued Feb. 5, 1991 to M. Karakelle et al.). Of the several functional coalings disclosed in the '357 patent, the coalings containing poly- (ethylene oxide) are useful herein for coaling the loons. Suitable coatings are uniform blends of an elastomeric segmented hydrophilic poly(urethanes) (HPEU) and poly(elthylene oxide) in an equeous Examples of other useful functional polythermoplastic tubing used to form dilatation balliquid. The poly(ethylene oxide) should be present in an amount of about 5 to 25 wt. %.

The HPEU is prepared from a cursoy service of projective rights of the curson and amino alcohol of up to 10 carbon atoms or mix-tures thereof. The polymer thus formed is prepared without the use of a catalyst and the resulting product is a polyurethane or a polyurethaneurea chain extender may be water and/or a low molecular weight branched or unbranched diol, diamine or The HPEU is prepared from a diisocyanate, depending upon the chain extender used.

32

Additional examples of useful functional polyo (ethylene oxide) coalings are found in U.S.
5,041,100 (issued August 20, 1991 to S.M. Rowland et al.), the disclosure of which is incorporated
herein by reterence. Of the poly(ethylene oxide)
coalings where the structural plastic is a thermoplastic, solvent-soluble linear polyurethane are useful for coaling the thermoplastic tubing used for of the polyurethane and 2 to 50 wt. % of a poly-(ethylene oxide) having a molecular weight of at least 10,000, preferably at least 1,000,000: Cost-ings which contain 10% to 30% poly(ethylene.oxforming dilatation balloons. These coatings comprise an intimate physical mixture of 50 to 98 wt. % ide) are most useful herein. Typically, an aqueous oxide) is used. There is no need for any curing step to effect cross-linking. The coatings provide at dispersion of the polyurethane and poly(ethylene east temporary lubricity and may be beneficially

20

EP 0 592 870 A1

BEST AVAILABLE COPY

employed in applications where temporary lubricity is sufficient or even desirable.

herein. The '607 coalings comprise an aqueous dispersion of a urethrane having a solids content of about 30-50% as the protective compound, a silicone or silicoxene emulsion having a solids content of at least about 15% as a site additive (e.g., dimethy siloxane), and optionally a crosslinking agent for the urethane (e.g., a polyfunctional aziridine). The disclosure of the above patents is user, previous presents of the Last State of the Other functional lubricious coatings useful herein include hydrophilic polyurethanes such as those disclosed in U.S. 4,156,066 and U.S. 4,156,067 (both issued May 22, 1979 to F.E. Gould); polyvinyl elcohols such as those disclosed are polyurethane polyester resins having free hydroxyl groups and carboxylate groups in the polymer backbone. The functional protective fubricious coatings disclosed in U.S. 5,028,607 (issued June 25, 1991 to M. Klezulas) are also useful

Incorporated herein by reference.

Many functional tubricious coating used in biomedical applications contain a significant amount of polyvinyl pyrrolidinone (PVP). It is examount of polyvinyl pyrrolidinone (PVP). pected that such coalings will be useful herein provided the PVP is adequately modified to accept the conditions of the expansion slep, for example, hrough the use of plasticizers, PVP copolymers, or other PVP modifiers.

coating additives include surfactants or wetting agents, viscosity and flow control agents, antioxidants, pigments, and air release agents or defeats, pigments, and air release agents or dederstood that certain coating additives commonly used in formulating coatings may be beneficially employed to produce a desirable result. Exemplary For all functional blomedical coatings, it is un-

\$

\$

Surfactants or wetting agents are used to promote wetting to the substrate as well as adhesion of the coeting to the substrate. Useful wetting agents include perfluoroalkyl ethoxylate mixtures. 2,4,7,9-tetramethyl 1-5-decyn-4,7-diol and ethylene oxide adducts thereof, 2,3,5-dimethyl-1, hexyn-3-ol, condensation products of ethylene oxide and di-(isohexyl-isoheptyl)phenol, condensation products.

20

Viscosily and flow control agents are used to of stearylamine and ethytene oxide, nonylphenox²² ypoly-(ethyleneoxy) ethanol, and polyethoxylated adjust the viscosity and thixotropy to a desired level. Preferably the viscosity is such that the coal-

A Company of Columns of

furned silica, cellulose acetate butyrate and ethyl acrystate/2-ethylhexyl acrystate copolymer. Flow confrol agents are preferably used in amounts from 0.05 to 5 wt. % of coating.

Antioxidants are used to improve the oxidative stability of the coatings and include but are not ing can be formed on the thermoplastic tubing at the desired thickness. Viscosities of from 50 cps to 500 cps can be used, although higher or lower viscosities may be useful in certain instances. Viscosity control agents include, but are not limited to.

hydroxybenzyl) benzene, butyl hydroxy toltene, cleadecyl 3,5-di-Lbutyl-4-hydroxyhydrocinnamate, 4,4-methylenebis(2,6-di-t butylphenol), p.p.-dioctyl diphenylamine, 1,1,3-tris-(2-methyl-4-hydroxy-5-t-butylphenyl) butane, Antioxidants are preferably used in amounts from 0,01 to 1 vs. % of coaling.

Conventional pigments can be added to impart color or radiopacity or to increase the desired limited, to tris (3.5-di-t-butyl-4-hydroxybenzyl)-isocyamurate, 2.2-methylenebis(4-methyl-6-l-butyl phenol), 1.3,5-trimethyl-2.4,6-tris(3.5-di-butyl-4-

52

0

appearance of the coatings.

2

Air release agents or detoamers are added to quickly release air bubbles formed in the wet film during the coating operation. They include, but are not limited, to polydimethyl siloxanes, 2.4.7.9 tetramethyl-5-decyn-4,7-diol, 2-ethylhexyl alcohol. 22

and n-beita-aminoethyl-gamma-amino-propyl-trimethoxysilane. Air release agants are often used in amounts from 0.005 to 5.0 % of the coating. Additionally, the functional bomedical coatings may also contain an effective amount of a thera-peutic agent which can diffuse out of the coating in

a continuous, controlled dosage over a substantial period of time.

streptokinase, urokinase, tissue plasminogen activator, anti-thromboxane B₂ agents, anti-B-thromboglobulin, prostaglandin E, aspirin, dipyridamole, anti-thromboxane A₂ agents, murine mornoclonal antibody 7E₃, triazolopyrimidine, ciprostene, Specific examples of such therapeutic agents include anti-thrombogenic agents or other agents for suppressing acute thrombosis, stenosis or late hirudin, ticlopidine, nicorandil, and the like. Antiplatelet derived growth factor may be used as a therapeutic agent to suppress subintimal fibromuscular hyperplasia at an arterial stenosis restenosis in arteries. Such agents include heparin, site, or any other inhibitor of cell growth at the stenosis site may be used.

\$

The therapeutic agent also may comprise a an antispasmodic agent such as papaverine. The therapeutic agent may be vasoactive agent such as vasodilator to counteract vasospasm, for example, calcium antagonists, or alpha and beta adrenergic

agent may comprise steroids for the purpose of with a controlled release carrier for persistence, to an infected stent or any other source of focalized The therapeutic agent may be an antibiotic which may be applied, optionally in conjunction infection within the body. Similarly, the therapeutic suppressing inflammation in a localized tissue site.

Also, anti-infective agents such as chlorhexidine may be added for improved infection resis-

tance of the coated product.

tenary ammonium compounds and/or amino-functional poly(ethylene oxide) to modify the release kinetics of therapeutic agents carried in the coating. The coating may contain binders such as qua-

ping, spraying, wiping, painting or the like. Preferaby, the tubing is dipped at about 20-25 °C and less than 60% relative humidity. Coating thickness and functionality can be affected by withdrawal rate typically applied using conventional methods. One end of the tubing is sealed and the outer surface of the coating mixture. The agents should be compati-The above functional biomedical coalings are the tubing is coated using a method such as dip-Care should be taken in adding other agents to ble with the functional agent and the agents used should not adversely affect each other's properties.

of the tubing from the coating mixture.

33

lowed to evaporate from the coated thermoplastic tubing, often by exposure to ambient conditions for a suitable drying time, typically from 15 to 480 minutes, or the tubing is dried at temperatures of 10 to 205°C from for from a few seconds to 48 hours. The time and temperature selected will, of course, depend upon the carrier used and the speed with which evaporation is desired. In all After applying the coating, the carrier is alcases the drying conditions should be non-deleterious to the underlying thermoplastic tubing.

stretching and expanding steps used in blow molding. One skilled in the art will select the proper The coated thermoplastic tubing is fabricated moplastic tubing coated and the type of functional into an expanded product using the conventional conditions, which will depend on the type of thercoating applied. In most cases, the stretched tubing is heated during stretching and expansion.

pared by blow molding, the process described in U.S. Re. 32,383 (reissued July 11,1989 to S.B. suitable temperature a polymeric tubing having a finite length (L1) and an internal diameter (ID1) to a Levy) is typically used. The process described in '983 patent is carried out by drawing at a length (L2) which is 3 to 6 Li, then expanding the When a coaled dilatation balloon is being pre-

tube being coaxially disposed within the second tube in such a manner that the second tube sur-rounds the first tube. Near the distal end of the

55

lubing during the expansion step. If the tubing extends beyond the mold, the use of a restraining means is preferred to maintain the dimensions of ture. A suitable temperature is one within the range extending from the second order transition temperature to the first order transition temperature to Similar temperatures can be used for both the drawing and expanding steps. The desired temperature can be achieved by any suitable heat generating means. For polyethylene terephthalate (PET) the preferred temperature is 84-89 °C. For polyurethanes the temperature will vary depending upon the polyurethane's composition and the deconventional equipment. A mold having a cavity with dimensions commensurate with the desired a suitable fitting so that a pressurized fluid (e.g., a gas such as nitrogen) can be introduced into the tubing. After the drawn tubing is positioned in the thermoplastic polymer used for the tubing. ID, followed by cooling the drawn and expanded tubing to less than the second order transition temperature. The process can be carried out in used. The open end of the tubing is equipped with the tubing in the region outside the mold while the pressure is being applied to the inside wall of the mold, heat is applied to raise the tubing's temperadrawn tubing of internal diameter (ID.) which is 6-8 of the balloon to be produced is typically sired characteristic of the final product. Size ž

It will understood by one skilled in the art that some adjustments in the drawing and expansion ratios and in the drawing and expansion temperatube drawing step is typically performed prior to the tube expansion step, the latter can be per-formed immediately after the drawing of the tubing. tures may be necessary to fabricate balloons. One skilled in the art will recognize that, although the or it can be performed at a later time.

Because of the recovery characteristics of shaped polymeric structures which are drawn by maintain axial tension on the drawn tubing during necessary to the above procedures, it may be the expansion step.

The coated balloons are attached to the cathking adhesives, hot melt adhesives, plastic welding, eters using conventional methods such as crosslin-

\$

al.). The assembly is formed of two heat-shrinkable. Irradiated modified polyolelin tubes: with the first The present process can be used to coal the inflatable annular portion of integral dilatation catheters such as the combination guiding catheter-4,323,071 (issued April 6, 1982 to J.B. Simpson el or the like. Typically, the catheters are not coated. ditating catheter assembly described

ŝ

BEST AVAILABLE COPY

EP 0'592 870 A1

heated along its length in a suitable manner, such as by a hot air tool to a suitable temperature of about 120°. The second tube shrinks and forms a tight seal with respect to the first tube. Alternative methods for forming the calheter are disclosed in tional biomedical coatings can be used and the nutar portion to permit the introduction of an expansion fluid into the balloon-like portion for inflating the '071 patent, the disclosure of which is incorporated herein by reference. Alternatively, the entire second tube of the combination can be coated balloon can then be inflated in the conventional between the second tube and extends from the proximal end into the balloon-like or inflatable anthe balloon-like portion and for withdrawing the expansion fluid to deltate the balloon-like portion. The second tubular member is then progressively instead of just the baltoon. Any of the above funcannutar portion. An annular Ilow passage is formed

5

illustrative and that other embodiments and modifications may be apparent to those skilled in the art It should be understood that the foregoing description of the invention is intended merely to be without departing from the spirit of the invention.

22

Example 1

a. Preparation of Premix

solution was not uniform (i.e., if any lumps or gels were present), the lumps or gels were broken up and the solution was allowed to stand for 24 hours. The solution was then rolled for about 60 minutes of methylene chloride about 132 g. of a poly-(ethylene oxide) marketed under the trade name POLYOX® WSR N-750 NF resin: The POLYOX® chloride was prepared by adding to about 3868 g. Registry No. 25372-68-3) with an approximate molecular weight of 300,000. The mixture was rolled at A poly(ethylene oxide) premix in methylene WSR N-750 NF resin is a water-soluble resin (CAS 6-10 rpm for at least 24 hours. If the resulting to form a uniform solution of 3.3 wt. % total solids.

b. Preparation of Coating

from the Costings Division of Miles Corp. Multron
F18.18.10/lystler.resin.having a hydroxyl.number
of 57-63, acid number of 1.2 maximum, water con-The final coating was prepared by adding a polyester polyol and an aromatic poly(isocyanate) tent of 0.10 wt. % maximum, Gardner color of No. 2 maximum, and viscosity at 73°C of 900-1600 mPa's. Typically, the colorless to light yellow liquid has a OH content of 1.8%, average equivalent polyol used was Multron..R-18. which is available to the poly(ethylene oxide) premix. The polyester

weight of 935, specific gravity of 1.19 @ 5.C, weight per gallon of 9.9 lbs., viscosity @ 20.C of 26,000 mPa's, and flash point (Pensky-Marten closed cup) of 204.C (400.F). The isocyanate used was Mondur CB-60 which is available from the Coatings Division of Miles Corp. Mondur CB-60 is an aromatic polyisocyanate adduct based on NCO content of 10.0 - 10.8%, Gardner color of No. 4 maximum, viscosity @ 20 · C of 150-600 mPa's. and free TDI monomer content of 0.7% maximum. Typically, the clear, slightly yellow liquid has an @ 25 C of 1.13, weight of 9.4 lbs. per gallon, and (25:15). It has a solids content of 60 ± 2 wt. %, equivalent average weight of 404, specific gravity totuene diisocyanate (TDI) dissolved in propytene glycol monomethyl ether acetate (PMA) and xylene flash point of 28 °C (82 °F).

A total of 6.72 g. of the polyester polyol was added to an appropriately sized container. Then 3.22 g. of the isocyanate were added, followed by 265.3 g. of the poly(ethylene oxide) premix and then by 421.7 g. of methylene chloride. The resulting mixture was mixed on a roller for at least 5 minutes and until it was visually homogenous. The coating solution had a total solids content of about

2

c. Application of the Coating

distortion temperature. D-1044 (or Taber abasion. D-1043 for Clash-Berg modulus, and D-790-for polyether polyurethane resin used for extrusion and injection molding. Typically, it has a melt index of about 34 gm/d min. (224. c, 5000 gp.) burometer D hardness of 74 ± 4; specific gravity of 1.21; tensile modulus of 165,000 psi; ultimate tensile strength of 6990 psi; ultimate lengiles. and outer dimensions ranging from 0.0151 to 0.0476 were heat sealed at one end. The tubing used was PELLETHANE® 2363-75D available from Dow Chemical Co. PELLETHANE® 2363-75D is a weight, 1000 cycles) of S5 mg. loss; Clash-Berg Modulus (TI) of +9 °C; and flexural modulus ~ 190,000 ps; The ASTM test metriodS used are as fornows; D-i238 for melt Index; D-2240 for hard-Thermoplastic polyurethane tubings having inner diameters ranging from 0.0077 to 0.0238 inwell thicknesses ranging from 0.0037 to 0.0119 inwell thicknesses ranging from 0.0037 to 0.00119 inwell thicknesses ranging from 0.0037 to 0.0038 inwell thicknesses ranging from 0.0037 to 0.00 tear strength (Die C) of 14 pli; heat distortation temperatures of 65 and 55 at 66 and 264 psi. respectively; Taber abrasion (H-22 wheel, 1000 g. ness; D-792 for specific gravity; D-412 for tensile modulus, ultimate tenule strength and ultimate elongation; D-624 for tear strength; D-648 for heat 20 35 \$ 8

The coating was applied by dipping the tubing in the above solution. The tubing was introduced at a rate of about 25 inches per minute and withdrawn

Evaluation of the Coating on the Tubing

The surface of the tubing contained a continuous coating of a crosslinked polyurethane complexed or associated with polyfellinylene oxide). When viewed under an optical microscope, the smooth coating was observed to be free from fissuring, crazing or other signs of coating rupture.

5

Sungle craims of control and a control and a cost a aqueous solution of Congo Red. The solution was popured into an appropriately sized and shaped cylinder. The coaled tubing to be tested was immersed in the solution for approximately 30 seconds. The tubing was then held under running tap was a marked line of distinction where the coated portion of the tube met the uncoated section, as demonstrated by the red color. The tubing was then wiewed under 20X magnification. A continuous then weed under 20X magnification. A continuous

red film was observed.

The wet coating on the tubing exhibited a high degree of lubricity as determined by tubbing the coated tubing between the fingers white applying a firm pressure, and comparing the ease of movement to that observed when performing the same test on a similar wet tubing which had not been coated. The uncoated tubing, even when wet, offered significantly more resistance to movement than the coated tubing.

8

The abrasion resistance of the coaling was determined by placing the coaled, stained tubing under a stream of running lap weter again so that the coaling would be rehydrated. While under the running wear, the tubing was rubbed between the finger and thumb for a total of 20 times while applying firm finger pressure. After this, the coaling still exhibited a continuous red color along the tubing, indicating that it did not wear off. Further examination for tubing given the above abrasion test the section of tubing given the above abrasion test was the same as a similar section that was not

The integrity of the coating after the abrasion test was further verified by allowing the coated tubing to dry and reexamining the coated surface under a 50 X optical microscope. A continuous, unundured coating was observed.

9

The coaled fubling was then subjected to to-focycles of wetting, lubricity testing, and drying. If was found that the lubricity did not change even after 10 wetting and drying cycles.

The lubricity was further tested by determining

the coefficient of friction using a procedure based

on ASTM D-1894. In this test, five uncoated pieces of the thermoplastic tubing were affixed parallel to a stationary platform. The platform with the pieces attached was immersed in 39° C water. A sled (200 gram stainless steel wrapped in tatex rubber) was attached to a load cell and frantser mechanism. The sled was placed on the samples and pulled across the surface of the tubing at a rate of six inches per minute. The force (both stalfic and kinches per minute. The force (both stalfic and kinches per minute. The force (both stalfic and kinches) required to pull the stalf was recorded. The control tubings were replaced with the coated thermoplastic tubings, and the test was rerun. Once again, the force (both stalfic and kinclic) required to pull the stad was recorded. The coated tubes showed a consistent decrease in friction of approximately 50%.

e. Formation of the Balloon

2

Balloons were then formed as follows. The coated polyurethane tubings were placed in a mold which has a cavily with dimensions equivalent to the desired size of the balloon to be formed. The non-sealed end of the coated tubings were times while applying firm finger pressure. Clamps were times while applying firm finger pressure. After this, the coating still exhibited a continuous red color elong the balloon, indicating that it did not wear off. Further examination for lubricity showed that the lubricity of the section of balloon given the above abrasion test was the same as a similar section that was not rubbed.

32

The integrity of the coating effer the abrasion lest was further verified by allowing the coated tubing to dry and reexamining the coated surface under a 50x optical microscope. A continuous, unruptured coating was observed.

35

Example 2

\$

A tubing measuring 0.017 in. in inner diameter and having an outer diameter of 0.0315 in. was coated and formed into a balloon using the procedure of Example 1. When inflated the balloon measured 0.100 in. in diameter atong a central cylindrical section 0.740 in. long. There were conical sections at each end, tapening at one and from 0.100 in. in diameter to 0.034 in. atong a length of approximately 0.165 in. at one end and taperting at the other and from 0.100 in. in diameter to 0.040 in. along a length of approximately 0.165 in. at the other and The wall thickness of the balloon in the conter cylindrical portion-was about 0.001 in.

ž,

center cylindrical portion, was about U.U.U. In.

If The process of forming the balloon, the coatesterminates an asset of surface of the tubing underwent a radial expansion of axial expansion.

Of axial expansion.

The surface of the balloon contained a continuous coating of a crosslinked polyurethane polytelthane oxides complex. When viewed under 30 X optical microscope, a smooth coating was observed, tree from fissuring, crazing or other sign of coating rupture. The coating continuity was further disclosed by staining the coating, by immersing the coated baltoon in 0.5% aqueous Congo Red solution for 20 seconds, followed by rinsing in 1ap water to remove excess Congo Red. A continuous red film was observed, corresponding to the coat-

ing, which absorbs the dye.

The wet coaling on the balloon exhibited a high degree of lubricity as determined by rubbing the coated balloon between the lingers while applying a firm pressure, and companing the base of movement to that observed when performing the seme test on a similar wet balloon which did not contain a coaling. The uncoated balloon, even when wet, offered significantly more resistance to movement than the coated balloon.

The durability of the coaling was determined by placing a coated, stained balloon under a stream of unming tap water and nubbing the coaling between the finger and thumb for a total of 20 times while applying firm linger pressure After this, the coating still exhibited a continuous red color along the balloon, indicating that it did not wear off. Further examination for tubricity showed that the lubricity of the section of balloon given the above abrasion test was the same as a similar section

that was not rubbed.

The integrity of the coating after abrasion test was further verified by allowing the balloon to dry. and reexamining the coated surface under a 30 X optical microscope. A continuous, unruptured coal-

The coated balloon was then subjected to 10 cycles of wetting, lubricity testing, and drying. It was found that the lubricity observed did not change even after 10 wetting and drying cycles.

cample 3

A coating formulation was prepared by weighing the following components into a disposable beaker:

ŧ

1) 3.61 grams of CB-60 (the isocyanale described in Example 1); soribed in Example 1); so 2.78 grams of a saturated polyester polyol

2) 2.78 grams of a saturated polyester polyol so (Multron R-12A, Miles Corporation) which typically has a hydroxyl content of 5%, equivalent yeagin (a 337, specific gravity © 20°C of 1.13 viscosity @ 20°C of 17.700 mPas, and ilash point (Pensky-Marten closed up) of 320°F ss

(1907-07).
3) 150 grams of a 3.3 wt. % methylene chloride solution of Polyox WSR N-750 (the poly-

(ethylene oxide) described in Example 1); and 4) 283 grams of methylene chloride. The components were thoroughly mixed with a spatula to produce a uniform coaling solution having total solids content of 2.25 vt. %.

The citing solution was then transferred to an 18 inch long glass tube heaving a 34 in outer diameter which was plugged at one end. The glass tube was used as a dippling vessel. Twelve inch lengths of polyethylene terephthatale tubing measuring 0.050 in. by 1.0 in. and having an outer diameter of 0.082 in. were plugged at the bottom diameter of 0.082 in. were plugged at the bottom of the purple was then dipped in the Tellon rod. The tubings were then dipped in the seconds. The tubings were then air dried at amplement conditions for a period of between 15 minutes and 120 minutes and then baked 8 hours at 50 °C to effect cure of the coaling. Continuous coalings to consisting of a crosslinked polyurethane complexed or associated with poly(ethylene oxide) were formed on the tubings.

The tubings were then formed into a dilatation balloon using the stretching, heating, and blow molding methods disclosed in U.S. Re. 32.833 (to S.B. Lavy). The tubings were heated at 180 °F and then simultaneously pressurized and stretched longinalizing and radially to form the balloons. The balloons were then heated for about 30-40 seconds at about 300 °F to crystallize the PET. The tinal balloons had a central crylindrical segment 1.10 in halloons had a central crylindrical segment 1.10 in halloons had a central crylindrical segment 1.10 in long a balloon and a contical section at each end. One conical section tapered from 0.320 in, to 0.100 in, along a length of 0.75 in. The other conical section tapered from 0.320 in, to 0.100 in, along a length of 0.75 in. The wall thickness of the coated balloons in the process so forming the balloon, the coated ed surface of the tubing underwent a radial expansion of 290%, as well as an indeterminate amount

There was a continuous coating on the surface of the balloon. The coated surface was viewed under a 30 X microscope and it was tee from fissuring, crazing or other signs of coating rupture. The coated balloons were tested for tubricity using the procedure of Example 2 and found to be very slippery when compared to an uncoated balloon having the same dimensions formed by the same process. The coated balloons were then subjected to durability lesting for coating integrity after fubricity desting. The ability of the coating integrity after fubricity cycles of weeting, lubricity (esting, and drying was also tested. The results were the same as was also tested. The results were the same as

BEST AVAILABLE COPY

A coating formulation was prepared by weighing the following components into a disposable

- 1.82 grams of CB-60 (the isocyante described
- 2) 3.86 grams of the polyester resin Multron R-18 (the polyester/polyol described in Example
- 3) 150 grams of 3.3 wt. % methylene chtoride solution of Polyox WSR N-750 (the poly-(ethylene oxide) described in Example 1); and
- components were mixed thoroughly with a spatula to produce a uniform coating solution hav-4) 284 grams of methylene chloride. 麏

ñ

tubing was air dried and cured using the conditions described in Example 3. The coating consisted of a crosslinked polyurethane complexed or associated The coating was applied to the polyethylene terephthalate tubing described in Example 3 using the same equipment and dip process. The coated ing a total solids of 2.25 wt. %..

2

The tubing was then formed into a dilatation balloon using the process described in Example 3. with poly(ethylene oxide).

ž

integrity after lubricity testing, and retained its lubricity after 10 cycles of wetting, lubricity testing, and drying as described in Example 2. A continuous coating was observed on the balloon surface. The coating became slippery when wetted with water. The coating exhibited durability, The balloon had the same dimensions.

Example 5

8

A coating formulation was prepared by weighing the following components into a disposable

lecular weight (M_w) of 124,000, and tensile @ break of 4000 psi and elongation at break of 750% at 1.5 Mil in MEK and tensile @ break of 3300 psi and elongation @ break of 760% at 1.5 B.F. Goodrich Corp.) which has a Brookfield viscosity of 260 cps. at 15% total solids in 15% total solids in cyclo hexanone; a Tg of 1) 115.7 grams of a 5 wt. % solution in methylene chloride of a thermoplastic polyesterurethane (Estane 5703F available from methyl ethyl ketone (MEK) and of 1600 cps. at -20 · C (DSC/second heat), a weight average momil in cyclohexanone.

£

8

(Polyox WSR N-60K; Union Carbide Corp.); and components were thoroughly mixed with 3) 55.7 grams of methylene chloride.

....

spatula to produce a uniform coating solution having a total solids content of 2.25 wt. %. The coating was a blend of the polyurethane and the high ratio of the polyurethane to poly(ethylene oxide) molecular weight poly(ethylene oxide). The weigh

terephthalate tubing described in Example 2 using The coaling was applied to the polyethylene the same process. A dilatation balloon was blown using the process described in Example 2. The

was microscopically reexamined under 30 X power and found to still have continuous coating. Presumably this was the Estane which was not altered by exposure to water, other than by the loss of some the coaled balloon exhibited a high degree of initial lubricity. However, the coating lost lubricity rapidly when rubbed with firm finger pressure under running water and became non-slippery after 5 rubring water. After lubricity testing, the surface of the balloon bing cycles. This was probably due to leaching of some of the poly(ethylene oxide) into the water. There was a continuous coating on the surface of the balloon, as indicated by microscopic examination under 30 X power. When wetted with water, of the admixed poly(ethylene oxide). balloon had the same dimensions.

Example 6

ing that the coating of Example 1 cannot be used This example is a comparative example show on a pre-formed polyurethane balloon.

in during 38 seconds as before. The balloon was air dried at ambient conditions for a period of about an hour and then baked 8 hours at 50°C to effect cure of the coating. The result was an adherent cure of the coating. the same dimensions as the balloon described in Example 3. The balloon end of the catheter was dipped into the coating solution to a depth of 9.5 The coating solution described in Example 3 was applied in a conventional manner. The distal end of a catheter shaft contained a pre-formed, coaling which exhibited good lubricity and durabilsignificant axial shrinkage in the balloon which This rendered the catheter useless as a medical was prepared. Instead of coating a length of polyethylene terephthalate tubing as before, the coating inflated polyethylene terephthalate balloon having ity when wetted with water. However, there was caused the catheter shaft to buckle in the region between the two adhesively bonded balloon ends.

\$

A coating formulation was prepared weighing 4.0 grams of a thermoplastic hydrophilic polyurethane polymer, available as D-6/40 from Tyndale

Plains-Hunter, Ltd., Ringoes, NJ into an eight ounce glass bottle. A total of 196 grams of methylene chloride was then weighted into the overnight to produce a uniform solution containing bottle, which was subsequently capped and rolled 2 wt. % of the polymer.

Tweive inch lengths of the polyethylene tereph thate tubing described in Example 3 were dip coated in this solution by Immersing them at about at ambient conditions for a period of 20-30 minutes and then baked at 100 °C for twenty minutes. The inches per second. The coated tubes were air dried tubes were then formed into a dilatation balloons as described in Example 3. The resulting dimensions then withdrawing them at a speed of about 0.25 inch per second to a depth of about 9 inches and expansion were as described therein.

2 25 X microscope the surface was observed to be free of fissuring, crazing or other sign of coating rupture. The balloon surface was wetted with water and found to be more lubricous than a similar gers. Lubricity was not diminished after twenty cycles of rubbing. The coating was stained in 0.5% aqueous Congo Red solution and it was found to over their entire surface. When viewed under a 30 The balloons exhibited a continuous coating uncoated balloon when rubbed between the finbe continuous and hydrophilic.

Example 8

35 \$ polytunctional aziridine crosslinker (available as KM10-1703 from Stahl Incorporated, Peabody, MA) into an 8 ounce glass bottle. A total of 195 grams dimethylsiloxane slip agent (available as UE-41-568 form Stahl Incorporated) was then weighed into the mulation was prepared by weighing 5.0 grams of a of a polyurethane emulsion containing a polybottle which was subsequently capped and rolled A non-hydrophilic protective slip-coating for-30 minutes to produce a uniform dispersion.

20 Ç Twelve inch lengths of the polyethylene tereph-thalate tubing described in Example 3 were dip coated as described in Example 7. The tubings were allowed to air dry at ambient conditions for a baked at 51.°C for 20 minutes to crosslink the polyurethane. The tubings were then formed into dilatation balloons as described in Example 3. The period of at least 5 minutes. Then the tubings were resulting dimensions and expansion were as described therein.

over their entire surface as evidenced by microscopic examination at 30 X. The dry balloon sur-The balloons exhibited a continuous coaling rubbed between the fingers, to feel slippery in face, which contained a significant amount of polydimethyl siloxane slip agent, was observed, when comparison to a similar uncoated balloon.

55

readily apparent to those skilled in the art. Accordingly, the spirit and scope of the present invention are to be limited only by the appended claims and that the preferred embodiments of the invention have been given in detail, various modifications and improvements thereon will become not by the foregoing specification. Now

Claims

 A process for preparing a coated expanded thermoplastic medical product, which comprises the steps of:

(a) applying to at least a portion of an inner and/or an outer surface of an expandable thermoplastic tubing at least one adherent prises at least one biomedical functional functional biomedical coating which comagent and a carrier,

5

time and temperature sufficient to remove at least part of the carrier; and (c) stretching and/or expanding the dried (b) allowing the coated tubing to dry at a

coated tubing with an inflating fluid at a pressure sufficient to form the coated expanded medical product. The process of Claim 1, further comprising the step of heating the partially dried coated tubing at a temperature and for a time sufficient to soften the coated tubing prior to stretching and/or expansion. બં

8

- ylene-butylene-styrene block copolymers admixed with low molecular weight styrene and optionally propylene; and polyether polyamide block copolymers and wherein the coating is a The process of Claim 1, wherein the tubing is ylene; polypropylene; polyethylene tereph-thelate; polybutylene terephthalate; polyvinyl ionomers; polyaryl ether ketones; polyureselected from the group consisting of polyeththane; ethylene-vinyl acetate copolymers; ethpolyetherimides polyamides; polyamideimides; polycarbonates; polyimides; ubricious coating. chloride; લ
- The process of Claim 3, wherein the substrate is polyurethane or polyethylene terephthalate and wherein the coating contains a poly-(ethylene oxide), a polyvinyl pyrrolidane, a hydrophilic polyurethane, or a silicone.
- The process of Claim 4, wherein the coating polymer selected from the group consisting of contains poly(ethylene oxide) a preformed polyurethane, a polyurea, and a polyurethane-urea or contains polymer precursors se-

- The process according to Claim 5, wherein the coating comprises a crosslinked polyurethane
- The uniformly functionally coated expanded thermoplastic medical product prepared by the process of Claim 1.

5

- The uniformly functionally coated expanded themoplastic medical product prepared by the process of Claim 3.
- The uniformly functionally coated expanded thermoplastic medical product prepared by the process of Claim 4.
- The uniformly functionally coaled expanded thermoplastic medical product prepared by the process of Claim 5.

2

11. The uniformly functionally coated expanded thermoplastic medical product prepared by the process of Claim 6.

35

- (a) applying to at least a portion of an inner and/or an outer surface of an expandable A process for preparing a coated balloon, which comprises the steps of: thermoplastic tubing at least one adherent lubricious coating which comprises at least one lubricious agent and a carrier;
- (b) altowing the coated tubing to dry at a least part of the carrier; and (c) stretching and/or expanding the dried coated tubing with an inflating fluid at a pressure sufficient to form the coated baltime and temperature sufficient to remove at

Ş

The process of Claim 12, further comprising the step of heating the partially dried coated tubing at a temperature and for a time sufficient to soften the coated tubing prior to stretching and/or expansion. 5

\$

chloride; — polyimides; — polyetherimides; paramentes; polyamides; 20 selected from the group consisting of polyetin-ylene; polypropylene; polyethylene tereph-thalate; polybutylene terephthalate; polyvinyl The process of Claim 12, wherein the tubing is ylene-butylene-styrene block copolymers ad-mixed with low molecular weight styrene and ionomers; polyaryl ether ketones; polyurelhane; ethylene-vinyl acetate copolymers; ethž.

- optionally propylene; and polyether polyamide block copolymers and wherein the coating is a lubricious coaling.
- The process of Claim 12, wherein the substrate is a polyurethane or polyethylene terephthate and wherein the coeting is a lubricious coating comprising a hydrophilic polyurethane and an organic solvent. ř
- The process of Claim 12, wherein the substrate is a polyurethane or polyethylene terephthaleie and wherein the coating is a proous dispersion of a urethane, a silicone or siloxane emulsion, and optionally a polyfunctective lubricious coating comprising an aquetional aziridine as a crosslinking agent.

15

- strate is a polyurethane or polyethylene terephthalate and coating contains poly-(ethylene oxide) and a preformed polymer sethane, a polyurea, and a polyurethane-urea or contains polymer precursors selected from the 17. The process of Claim 12, wherein the sublected from the group consisting of a polyuregroup consisting of polyurethane precursors and polyurea precursors.
- The process according to Claim 12, wherein the coating comprises a crosslinked polyure-. ≅

8

The coated balloon prepared by the process of ē;

32

- A process for preparing a lubricious dilatation balloon, which comprises the steps of:

 (a) applying to at least a portion of an outer surface of a thermoplastic lubing at least one adherent lubricious coating which comgroup consisting of a polyurethane, a mer precursors selected from the group prises (i) a carrier. (ii) a poly(ethylene oxide) dissolved, dispersed, or emulsified in the carrier, and (iii) a polymer selected from the polyurea, and a polyurethane-urea or polyconsisting of polyurethane precursors and polyurea precursors, the polymer or polymer precursors being dissolved, dispersed. 20.
 - (b) allowing the coated tubing to dry at a time and temperature sufficient to remove at or emulsified in the carrier;
- least part of the carrier; and (c) expanding with the costed tubing with the an inflating fluid in order to increase the diameter and length of the tubing white simultaneously orienting the tubing and for-

21. The process of Claim 20, wherein the orienting step includes heating the coated tubing to a the second order transition temperature to the temperature within the range extending from first order transition temperature of the thermoplastic polymer.

BEST AVAILABLE COPY

The process of Claim 21, further comprising the step of drawing the oriented section to provide a drawn oriented section, followed by expanding the drawn oriented section to a modified profile and size, further followed by heat setting the modified profile and size to form the coated balloon. 22

2

- 22 The process of Claim 20, wherein the tubing is selected from group consisting of polyethylene; polypropylene; polyethylene terephitialate; polybutylene terephitialate; polybutylene chloride; polyimides; polyetherimides; polyamides; polyamides; polyamides; polycarbonales; ionomers; polyaryl ether ketones; polyureylene-butylene-styrene block copolymers admixed with low molecular weight styrene and thane; ethylene-vinyl acetate copolymers; ethoptionally propylens; and polyether polyamide ដ
- The process of Claim 23, wherein the tubing is polyethylene terephihalate. ž

8

- The process of Claim 23, wherein the tubing is ķ
- 26. The process of Claim 23, wherein the tubing is a segmented polyurethane.
- The process of Claim 23, wherein the segmented polyurethane contains at least 45 wt.% of soft segments with the balance being hard 27.

\$

- £ The process of Claim 23, wherein the carrier is selected from the group consisting of water, methylene chloride, methylene bromide, trich-toroethylene, ethylene dichloride, N-methylpyrrolidone, pyridine, and mixtures thereof. ž
- S The process of Claim 23, wherein the polymer is polyurethane or polyurethane-urea which is prepared from a disocyanate, a polyether glycol, and a chain extender. 33
 - The process of Claim 29, wherein the sisting of water, a low molecular weight diol, a diisocyanate is methylene diisocyanate, the polyether glycol is polyethylene glycol, and the chain extender is selected from the group con-뛵

55

- or an amino alcohol of up to carbon atoms, and mixtures thereof.
- is an intimate physical mixture of about 50-98% by weight of a polyurethane and about 2-50% by weight of a poly(elhylene oxide) having a molecular weight of at least 10,000 in a 31. The process of Claim 23, wherein the coaling
- 32. The process of Claim 31, wherein the polyure-thane is a aliphatic polyurethane and the car-
- 33. The process of Claim 23, wherein the coating is a crosslinked polyurethane matrix associated or complexed with a poly(ethylene oxide).
- with a solution consisting essentially of an isocyanale, a polyol, and the polyethylene oxide dissolved in a suitable solvent. thane matrix is prepared by coating the tubing 34. The process of Claim 33, wherein the polyure-
- polyester polyols, polyacrylate polyols; wherein the poly(ethylene oxide) has a molecular weight of about 10,000-5,000,000 and wherein loroethylene, pyridine, n-methyle pyrrolidone, dioxolane, acetonitrile, and blends of the the solvent is selected from the group consist-The process of Claim 32, wherein the isocyanate is selected from the group consisting of 2,4- and 2,6-toluene diisocyante and disocyante and prepolymers thereof, diphenylmethane 4,4'-dilsocyante and prepolymers thereof, bis(4-isocyanatocyclohexyl) methane diisocyante and prepolymers thereof, wherein the polyol is selected from the group consisting of polyol selected from the group of castor oil and castor oil derivatives, saturated polyester polyols, polyether polyols, unsaturated dichloroethylene, trichand prepolymers thereof, and isophorone thereof, dibromomethane, prepolymers 35

ş

- The lubricious dilatation balloon prepared by the process of Claim 20. 36.
- an abrasion resistant. hydrophilic, lubricous coaling which is a continuous film of a crossmanners striked substantially polyurethane matrix comthe process of Claim 36, wherein the coating is The lubricious dilatation balloon produced by plexed or associated with a poly(ethylene oxide). 37.

28

EUROPEAN SEARCH REPORT

Application Number EP 93 11 5730

_		DOCUMENTS CONSIDERED TO BE RELEVANT	ANT	
1.5	Category	Citation of document with indication, where appropriate,	Relevant to claim	APPLICATION (INCLOS)
<u> </u>	>	EP-A-0 214 721 (FRÁNKLIN MEDICAL LIMITED) * column 4 - column 9; claims *	D) 1-38	A61L29/00 A61L33/00
-	>	EP-A-0 454 293 (C.R. BARD, INC.) * column 3, line 28 - column 6, line 48;	1-38	
	0	claims; examples * & US-A-5 077 352 (R. ELTON)		
	≺	WO-A-92 11877 (UNION CARBIDE CHEMICALS PLASTICS TECHNOLOGY CORPORATION) * claims *	4	
	≺ ⊂	EP-A-0 093 094 (ASTRA MEDITEC AB) A. IIS-A-4 459 317 (H. LAMBERT)		
	۸,0	US-A-5 026 607 (M. KIEZULAS)		
			 -	SEARCHED (BACLS)
				7E31L
			_	
		· . :		
			T	
		The present search report has been drawn up for all claims	-	, solid
· Cher		Fire of courts 10 January	1994 (Cousins-Van Steen, G
) (P04)		THE DOCUMENTS	T : theory or principle underlying the invention	the invention
1	1 13	1 11	filler date and	
DOG P	<u> </u>		D : document died in the application	997
1101		A technological hardground A tomobor A tomo	of the same putest	A : washer of the same patent family, corresponding document
141	_			

2

5

8

22